STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 168216

TO: Tamthom Truong **Location: rem/5B19/5C18** **Art Unit: 1624** **Thursday, October 13, 2005** **Case Serial Number: 10/786400**	**From: Paul Schulwitz** **Location: Biotech-Chem Library** **REM-1A65** **Phone: 571-272-2527** **Paul.schulwitz@uspto.gov**

Search Notes

Examiner Truong,

Please review the attached search results.
If you have any questions or if you would like to refine the search query, please feel free to contact me at any time.

Thank you for using STIC search services!

Paul Schulwitz
Technical Information Specialist
REM-1A65
571-272-2527

STIC SEARCH RESULTS FEEDBACK FORM

Biotech-Chem Library

Questions about the scope or the results of the search? Contact ***the searcher or contact*:**

Mary Hale, Information Branch Supervisor
Remsen Bldg. 01 D86
571-272-2507

Voluntary Results Feedback Form

- *I am an examiner in Workgroup:* ☐ *Example: 1610*
- *Relevant prior art **found**, search results used as follows:*
  - ☐ 102 rejection
  - ☐ 103 rejection
  - ☐ Cited as being of interest.
  - ☐ Helped examiner better understand the invention.
  - ☐ Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature
  (journal articles, conference proceedings, new product announcements etc.)

- *Relevant prior art **not found**:*
  - ☐ Results verified the lack of relevant prior art (helped determine patentability).
  - ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

Drop off or send completed forms to STIC-Biotech-Chem Library Remsen Bldg.

INVENTORS

L4 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:707163 HCAPLUS
DOCUMENT NUMBER: 133:266869
ENTRY DATE: Entered STN: 06 Oct 2000
TITLE: Preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors.
INVENTOR(S): Oxford, Alexander William; Jack, David
PATENT ASSIGNEE(S): Vanguard Medica Ltd., UK
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C07D471-04
SECONDARY: A61K031-519; C07D498-04; A61K031-553; A61P011-00; C07D471-04; C07D239-00; C07D221-00; C07D498-04; C07D267-00; C07D239-00
CLASSIFICATION: 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000058308	A1	20001005	WO 2000-GB1193	20000329
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
NZ 514158	A	20000329	NZ 2000-514158	20000329
CA 2368413	AA	20001005	CA 2000-2368413	20000329
AU 2000041274	A5	20001016	AU 2000-41274	20000329
AU 773504	B2	20040527		
EP 1165558	A1	20020102	EP 2000-920857	20000329
EP 1165558	B1	20030924		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000009446	A	20020115	BR 2000-9446	20000329
JP 2002540207	T2	20021126	JP 2000-608010	20000329
AT 250602	E	20031015	AT 2000-920857	20000329
PT 1165558	T	20040227	PT 2000-920857	20000329
ES 2208310	T3	20040616	ES 2000-920857	20000329
US 2003036542	A1	20030220	US 2001-964260	20010926
US 6794391	B2	20040921		
NO 2001004728	A	20011123	NO 2001-4728	20010928
US 2004171828	A1	20040902	US 2004-786650	20040224
US 2004176353	A1	20040909	US 2004-786400	20040224

parent → US 6794391

→ process of making

<-- method

PRIORITY APPLN. INFO.:

GB 1999-7454	A	19990331
GB 1999-9802	A	19990428
WO 2000-GB1193	W	20000329
US 2001-964260	A3	20010926

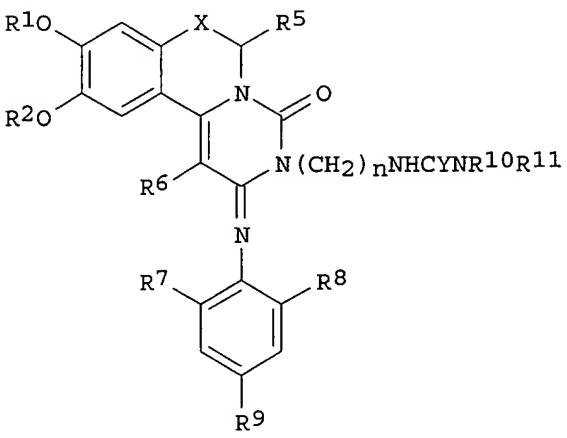
PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES

WO 2000058308	ICM	C07D471-04
	ICS	A61K031-519; C07D498-04; A61K031-553; A61P011-00; C07D471-04; C07D239-00; C07D221-00; C07D498-04; C07D267-00; C07D239-00
WO 2000058308	ECLA	C07D471/04+239C+221C
US 2003036542	NCL	514/211.120
	ECLA	C07D471/04+239C+221C
US 2004171828	NCL	540/548.000
	ECLA	C07D471/04+239C+221C
US 2004176353	NCL	514/211.120
	ECLA	C07D471/04+239C+221C <--

OTHER SOURCE(S): MARPAT 133:266869

GRAPHIC IMAGE:



I

ABSTRACT:
Title compds. [I; R1, R2 = alkyl, acyl; R5 = H, alkyl, alkenyl, alkynyl; R6 = H, alkyl, alkenyl, alkynyl, amino, alkylamino, dialkylamino, acylamino; R7, R8 = H, halo, OH, CF3, alkyl, alkenyl, alkynyl, acyl, alkythio, alkoxy, cycloalkyl; R9 = H, halo, OH, CF3, alkyl, alkenyl, alkynyl, acyl, alkythio, alkoxy, cycloalkyl; X = OCH2, CR3R4; R3, R4 = H, alkyl; R10, R11 = H, alkyl, cycloalkyl, Ph; Y = O, CHNO2, NCN, NH, NNO2; n = 2-4], were prepared I have a longer duration of action than the known compound trequinsin (9,10-dimethoxy-3-methyl-2-mesitylimino-2,3,6,7-tetrahydro-4H--pyrimido[6,1-a]isoquinolin-4-one) and do not have trequinsin's very bitter taste. Thus, Na cyanate was added dropwise to 9,10-dimethoxy-2-(2,4,6-trimethylphenylimino)-3-(2-aminoethyl)-3,4,6,7-tetrahydro-2H-pyrimido[6,1-a]isoquinolin-4-one (preparation given) in aqueous
HCl at 80° followed by stirring for 2 h to give 54% 9,10-dimethoxy-2-(2,4,6-trimethylphenylimino)-3-(N-carbamoyl-2-aminoethyl)-3,4,6,7-tetrahydro-2H-pyrimido[6,1-a]isoquinolin-4-one(II). II inhibited PDE3 with IC50 = 0.46 μM and was tasteless.

SUPPL. TERM: aryliminopyrimidoisoquinolinone prepn phosphodiesterase inhibitor; pyrimidoisoquinolinone arylimino prepn phosphodiesterase inhibitor; chronic obstructive pulmonary disease treatment aryliminopyrimidoisoquinolinone prepn; antiasthmatic aryliminopyrimidoisoquinolinone prepn; bronchodilator aryliminopyrimidoisoquinolinone prepn

INDEX TERM: Lung, disease

(chronic obstructive, treatment; preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)

INDEX TERM: Antiasthmatics
Bronchodilators
Cytotoxic agents
(preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)

INDEX TERM: Proliferation inhibition
(proliferation inhibitors; preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)

INDEX TERM: Tumor necrosis factors
ROLE: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(release inhibitors; preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)

INDEX TERM: 9036-21-9, Phosphodiesterase III
ROLE: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(inhibitors; preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)

INDEX TERM: **298680-25-8P 298680-26-9P**
298680-27-0P 298680-28-1P
298680-29-2P 298680-30-5P
298680-31-6P 298680-32-7P
298680-33-8P 298680-34-9P
298680-35-0P 298680-36-1P
298680-37-2P
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)

INDEX TERM: 62-56-6, Thiourea, reactions 75-31-0, Isopropylamine, reactions 88-05-1, 2,4,6-Trimethylaniline 95-53-4, 2-Methylaniline, reactions 103-71-9, Phenyl isocyanate, reactions 574-98-1, N-(2-Bromoethyl)phthalimide 1795-48-8, Isopropyl isocyanate 2260-00-6 3173-53-3, Cyclohexyl isocyanate 5394-18-3, N-(4-Bromobutyl)phthalimide 10191-60-3, Dimethyl N-cyanodithioiminocarbonate 13623-94-4 24544-04-5, 2,6-Diisopropylaniline 61832-41-5 **298680-49-6**
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)

INDEX TERM: 2986-25-6P **75535-96-5P 76536-66-8P**
145013-05-4P **214358-62-0P 298680-38-3P**
298680-39-4P 298680-40-7P
298680-41-8P 298680-42-9P
298680-43-0P 298680-44-1P
298680-45-2P 298680-46-3P
298680-47-4P 298680-48-5P
298680-50-9P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)

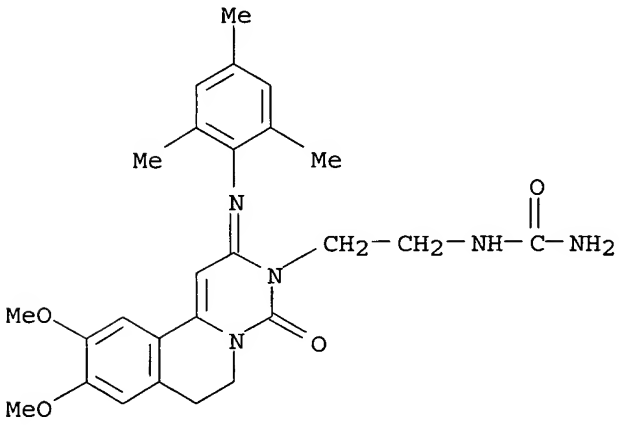
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S): (1) Bansai, L; JOURNAL OF MEDICINAL CHEMISTRY 1984, V27(11), P1470

IT **298680-25-8P 298680-26-9P 298680-27-0P**
298680-28-1P 298680-29-2P 298680-30-5P
298680-31-6P 298680-32-7P 298680-33-8P
298680-34-9P 298680-35-0P 298680-36-1P
298680-37-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)

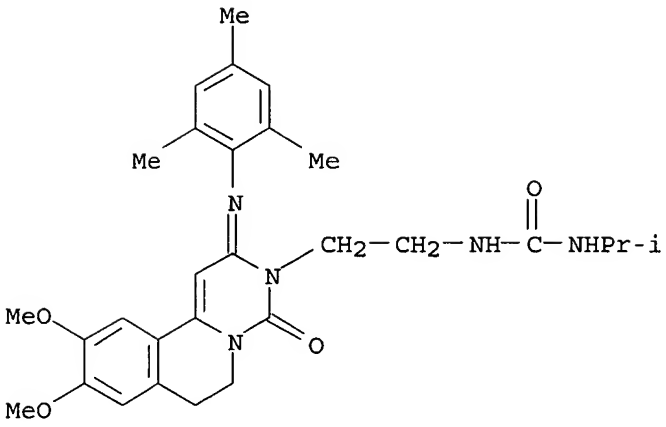
RN 298680-25-8 HCAPLUS

CN Urea, [2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)

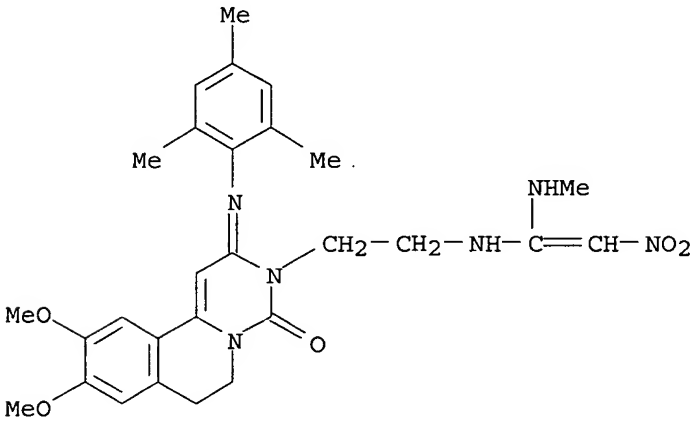


RN 298680-26-9 HCAPLUS

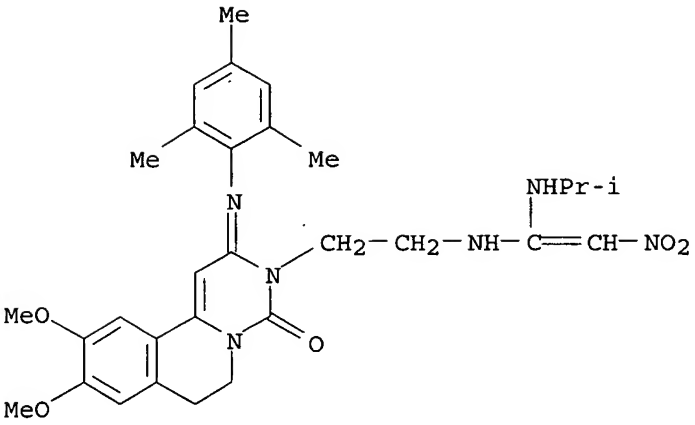
CN Urea, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-(1-methylethyl)- (9CI) (CA INDEX NAME)



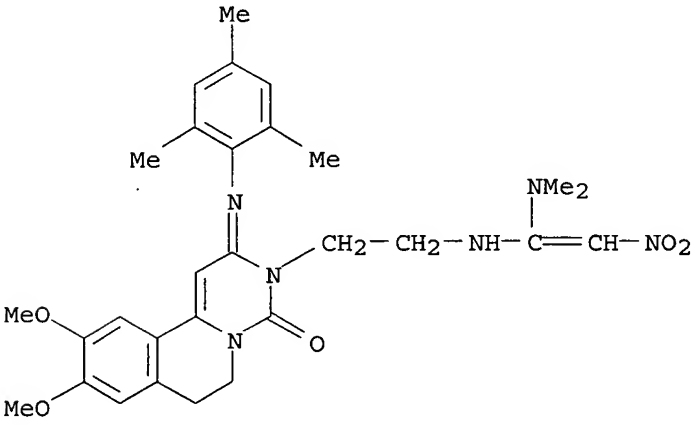
RN 298680-27-0 HCAPLUS
CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 2,3,6,7-tetrahydro-9,10-dimethoxy-3-[2-[[1-(methylamino)-2-nitroethenyl]amino]ethyl]-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)



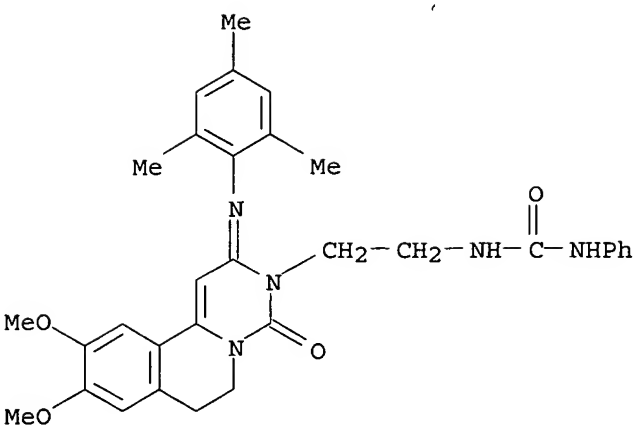
RN 298680-28-1 HCAPLUS
CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 2,3,6,7-tetrahydro-9,10-dimethoxy-3-[2-[[1-[(1-methylethyl)amino]-2-nitroethenyl]amino]ethyl]-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)



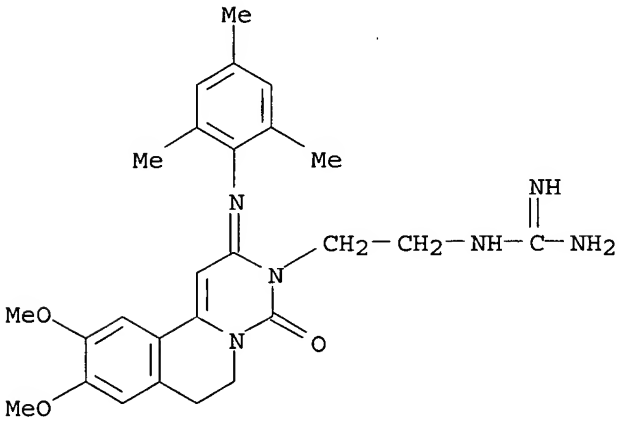
RN 298680-29-2 HCAPLUS
CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 3-[2-[[1-(dimethylamino)-2-nitroethenyl]amino]ethyl]-2,3,6,7-tetrahydro-9,10-dimethoxy-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)



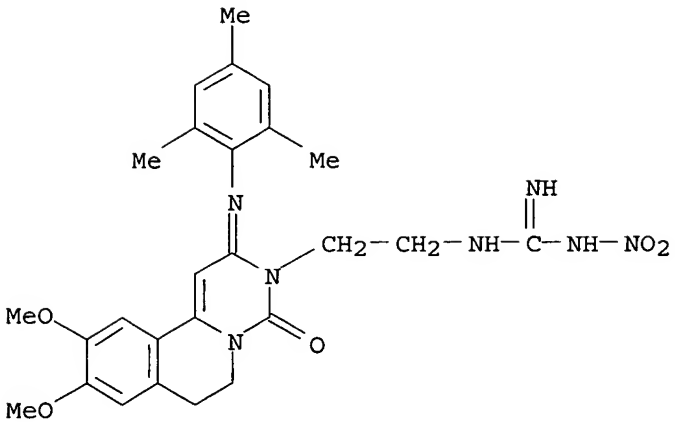
RN 298680-30-5 HCAPLUS
CN Urea, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-phenyl- (9CI) (CA INDEX NAME)



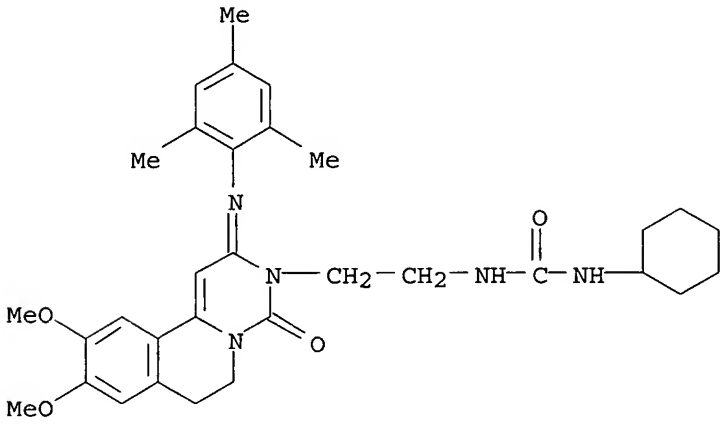
RN 298680-31-6 HCAPLUS
CN Guanidine, [2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-(9CI) (CA INDEX NAME)



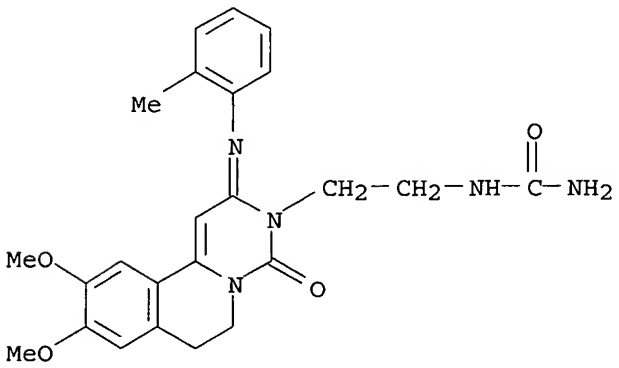
RN 298680-32-7 HCAPLUS
CN Guanidine, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-nitro- (9CI) (CA INDEX NAME)



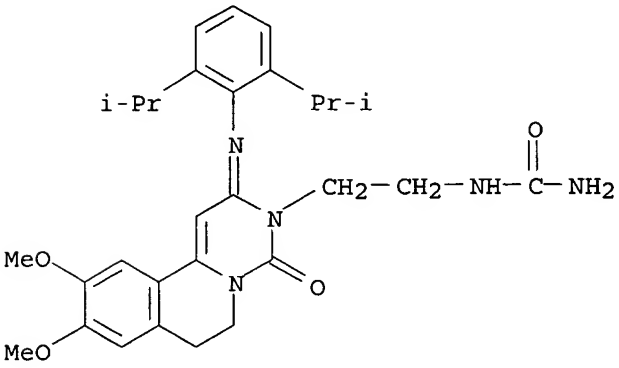
RN 298680-33-8 HCAPLUS
CN Urea, N-cyclohexyl-N'-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)



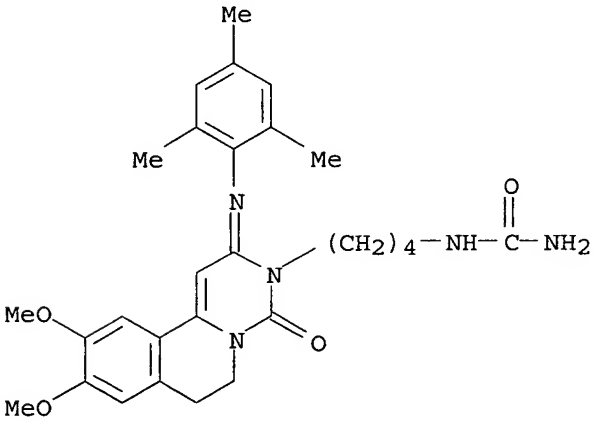
RN 298680-34-9 HCAPLUS
CN Urea, [2-[6,7-dihydro-9,10-dimethoxy-2-[(2-methylphenyl)imino]-4-oxo-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)



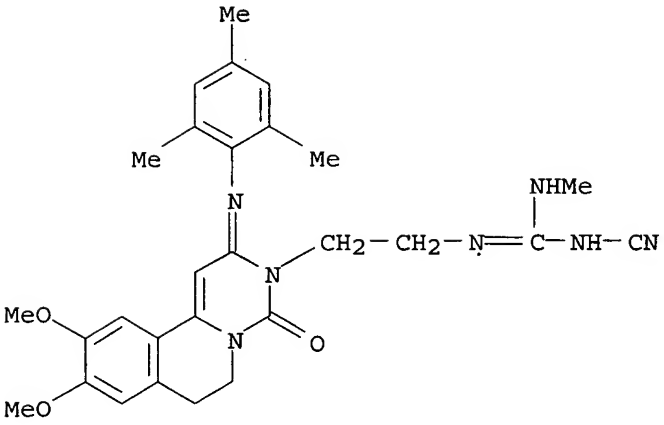
RN 298680-35-0 HCAPLUS
CN Urea, [2-[2-[[2,6-bis(1-methylethyl)phenyl]imino]-6,7-dihydro-9,10-dimethoxy-4-oxo-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)



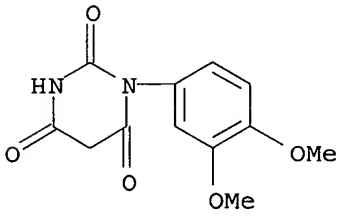
RN 298680-36-1 HCAPLUS
CN Urea, [4-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]butyl]- (9CI) (CA INDEX NAME)



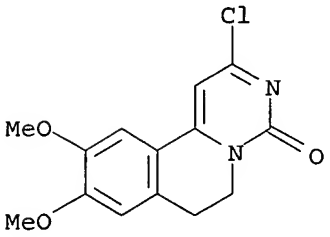
RN 298680-37-2 HCAPLUS
CN Guanidine, N-cyano-N'-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N''-methyl- (9CI) (CA INDEX NAME)



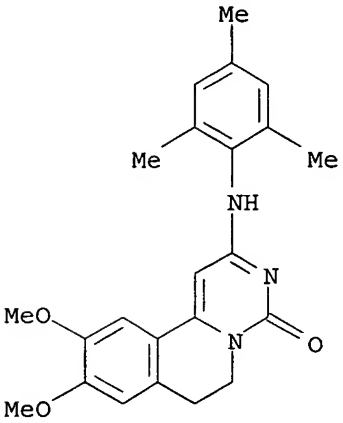
IT **298680-49-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)
RN 298680-49-6 HCAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 1-(3,4-dimethoxyphenyl)- (9CI) (CA INDEX NAME)



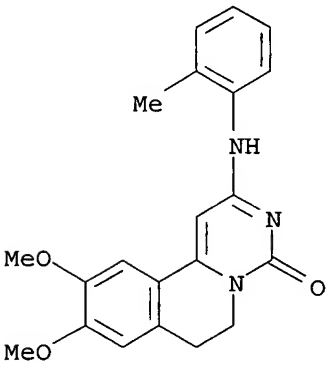
IT **75535-96-5P 76536-66-8P 214358-62-0P**
298680-38-3P 298680-39-4P 298680-40-7P
298680-41-8P 298680-42-9P 298680-43-0P
298680-44-1P 298680-45-2P 298680-46-3P
298680-47-4P 298680-48-5P 298680-50-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)
RN 75535-96-5 HCAPLUS
CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 2-chloro-6,7-dihydro-9,10-dimethoxy- (9CI) (CA INDEX NAME)



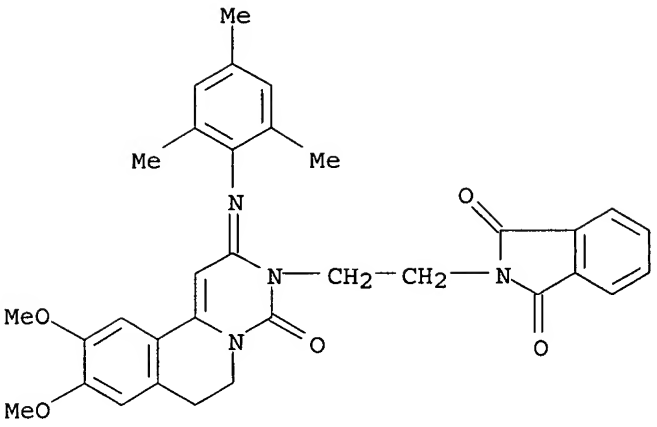
RN 76536-66-8 HCAPLUS
CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 6,7-dihydro-9,10-dimethoxy-2-[(2,4,6-trimethylphenyl)amino]- (9CI) (CA INDEX NAME)



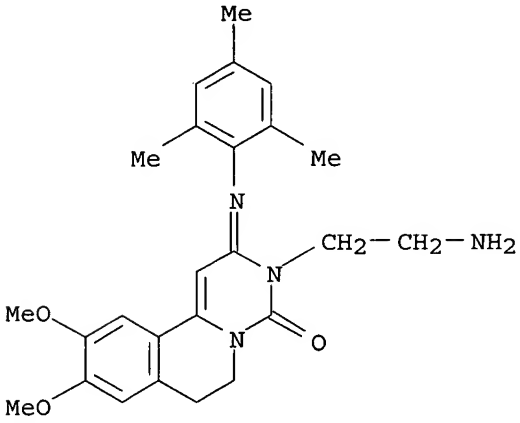
RN 214358-62-0 HCAPLUS
CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 6,7-dihydro-9,10-dimethoxy-2-[(2-methylphenyl)amino]- (9CI) (CA INDEX NAME)



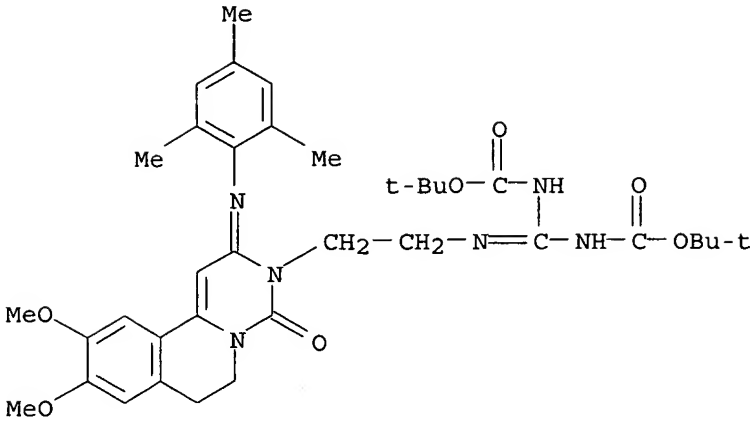
RN 298680-38-3 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)



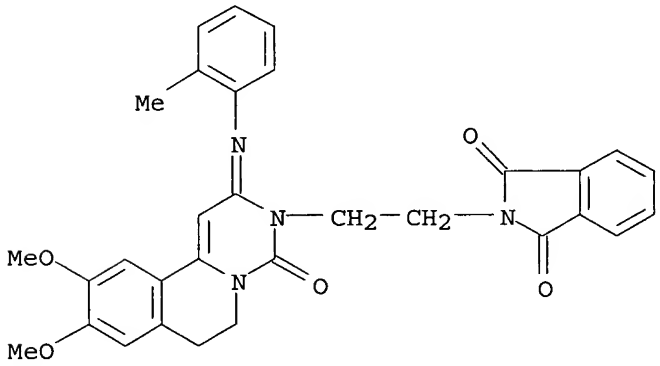
RN 298680-39-4 HCAPLUS
CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 3-(2-aminoethyl)-2,3,6,7-tetrahydro-9,10-dimethoxy-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)



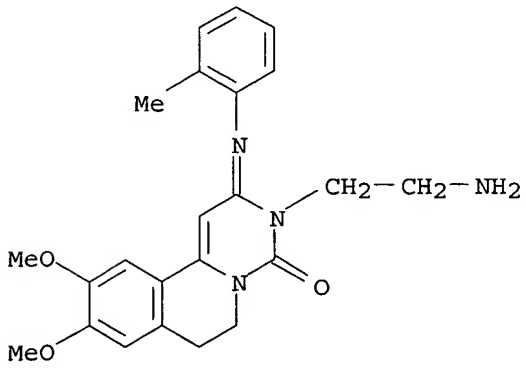
RN 298680-40-7 HCAPLUS
CN Carbamic acid, [[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]carbonimidoyl]bis-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



RN 298680-41-8 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[6,7-dihydro-9,10-dimethoxy-2-[(2-methylphenyl)imino]-4-oxo-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)

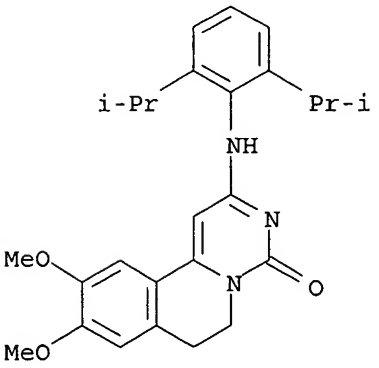


RN 298680-42-9 HCAPLUS
CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 3-(2-aminoethyl)-2,3,6,7-tetrahydro-9,10-dimethoxy-2-[(2-methylphenyl)imino]- (9CI) (CA INDEX NAME)

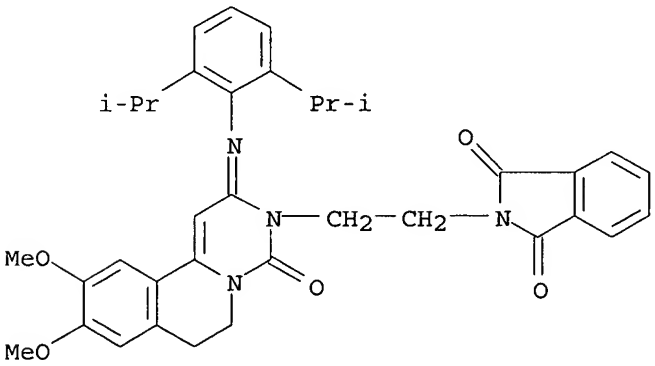


RN 298680-43-0 HCAPLUS

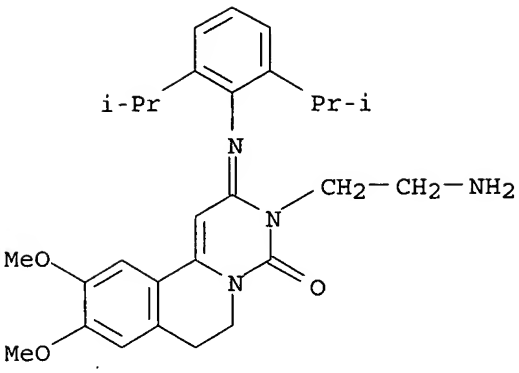
CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 2-[[2,6-bis(1-methylethyl)phenyl]amino]-6,7-dihydro-9,10-dimethoxy- (9CI) (CA INDEX NAME)



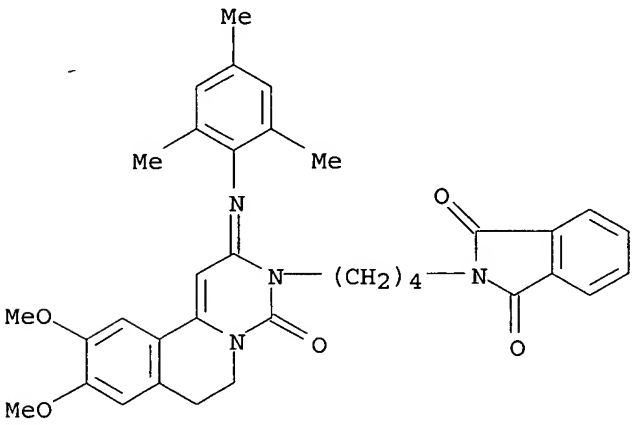
RN 298680-44-1 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[2-[[2,6-bis(1-methylethyl)phenyl]imino]-6,7-dihydro-9,10-dimethoxy-4-oxo-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)



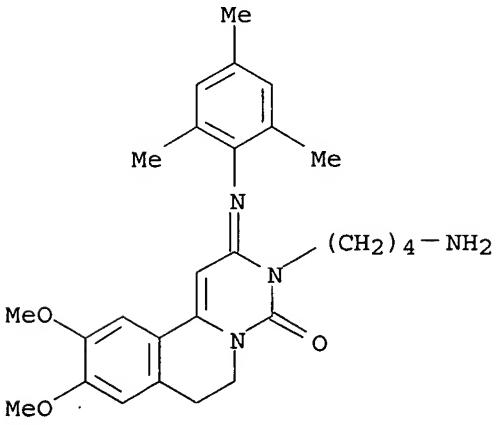
RN 298680-45-2 HCAPLUS
CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 3-(2-aminoethyl)-2-[[2,6-bis(1-methylethyl)phenyl]imino]-2,3,6,7-tetrahydro-9,10-dimethoxy- (9CI) (CA INDEX NAME)



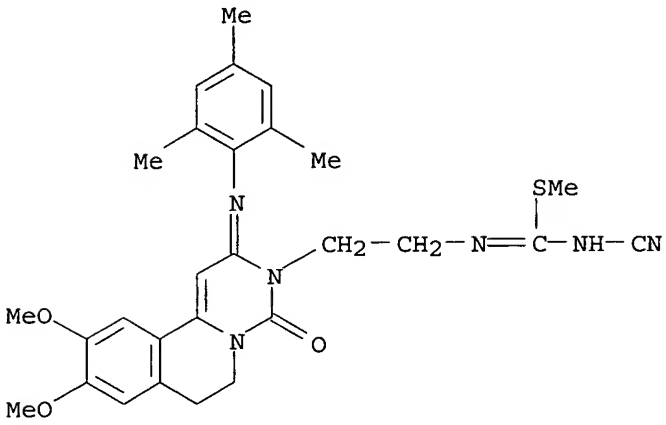
RN 298680-46-3 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[4-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]butyl]- (9CI) (CA INDEX NAME)



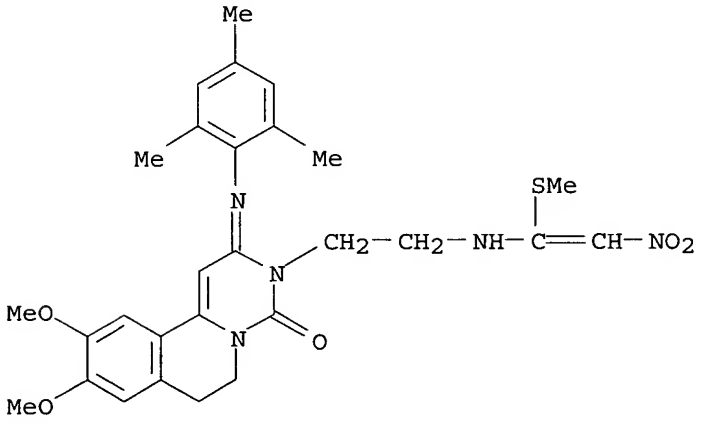
RN 298680-47-4 HCAPLUS
CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 3-(4-aminobutyl)-2,3,6,7-tetrahydro-9,10-dimethoxy-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)



RN 298680-48-5 HCAPLUS
CN Carbamimidothioic acid, N-cyano-N'-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 298680-50-9 HCAPLUS
CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 2,3,6,7-tetrahydro-9,10-dimethoxy-3-[2-[[1-(methylthio)-2-nitroethenyl]amino]ethyl]-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)



L4 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:707163 HCAPLUS
DOCUMENT NUMBER: 133:266869
ENTRY DATE: Entered STN: 06 Oct 2000
TITLE: Preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors.
INVENTOR(S): Oxford, Alexander William; Jack, David
PATENT ASSIGNEE(S): Vanguard Medica Ltd., UK
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C07D471-04
SECONDARY: A61K031-519; C07D498-04; A61K031-553; A61P011-00; C07D471-04; C07D239-00; C07D221-00; C07D498-04; C07D267-00; C07D239-00
CLASSIFICATION: 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000058308	A1	20001005	WO 2000-GB1193	20000329
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
NZ 514158	A	20000329	NZ 2000-514158	20000329
CA 2368413	AA	20001005	CA 2000-2368413	20000329
AU 2000041274	A5	20001016	AU 2000-41274	20000329
AU 773504	B2	20040527		
EP 1165558	A1	20020102	EP 2000-920857	20000329
EP 1165558	B1	20030924		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000009446	A	20020115	BR 2000-9446	20000329
JP 2002540207	T2	20021126	JP 2000-608010	20000329
AT 250602	E	20031015	AT 2000-920857	20000329
PT 1165558	T	20040227	PT 2000-920857	20000329
ES 2208310	T3	20040616	ES 2000-920857	20000329
US 2003036542	A1	20030220	US 2001-964260	20010926
US 6794391	B2	20040921		
NO 2001004728	A	20011123	NO 2001-4728	20010928
US 2004171828	A1	20040902	US 2004-786650	20040224
US 2004176353	A1	20040909	US 2004-786400	20040224 <--

PRIORITY APPLN. INFO.:		
GB 1999-7454	A	19990331
GB 1999-9802	A	19990428
WO 2000-GB1193	W	20000329
US 2001-964260	A3	20010926

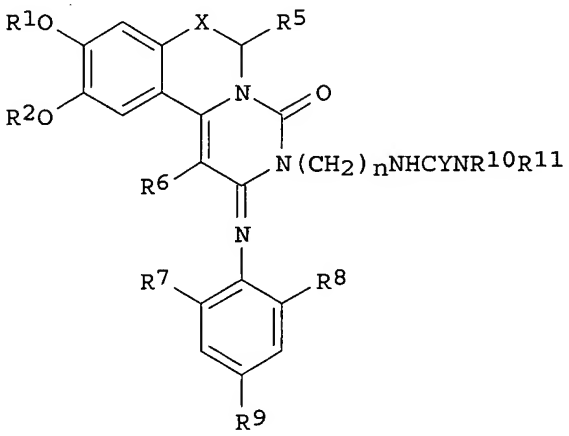
PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES

WO 2000058308	ICM	C07D471-04
	ICS	A61K031-519; C07D498-04; A61K031-553; A61P011-00; C07D471-04; C07D239-00; C07D221-00; C07D498-04; C07D267-00; C07D239-00
WO 2000058308	ECLA	C07D471/04+239C+221C
US 2003036542	NCL	514/211.120
	ECLA	C07D471/04+239C+221C
US 2004171828	NCL	540/548.000
	ECLA	C07D471/04+239C+221C
US 2004176353	NCL	514/211.120
	ECLA	C07D471/04+239C+221C <--

OTHER SOURCE(S): MARPAT 133:266869

GRAPHIC IMAGE:



I

ABSTRACT:
Title compds. [I; R1, R2 = alkyl, acyl; R5 = H, alkyl, alkenyl, alkynyl; R6 = H, alkyl, alkenyl, alkynyl, amino, alkylamino, dialkylamino, acylamino; R7, R8 = H, halo, OH, CF3, alkyl, alkenyl, alkynyl, acyl, alkythio, alkoxy, cycloalkyl; R9 = H, halo, OH, CF3, alkyl, alkenyl, alkynyl, acyl, alkythio, alkoxy, cycloalkyl; X = OCH2, CR3R4; R3, R4 = H, alkyl; R10, R11 = H, alkyl, cycloalkyl, Ph; Y = O, CHNO2, NCN, NH, NNO2; n = 2-4], were prepared I have a longer duration of action than the known compound trequinsin (9,10-dimethoxy-3-methyl-2-mesitylimino-2,3,6,7-tetrahydro-4H--pyrimido[6,1-a]isoquinolin-4-one) and do not have trequinsin's very bitter taste. Thus, Na cyanate was added dropwise to 9,10-dimethoxy-2-(2,4,6-trimethylphenylimino)-3-(2-aminoethyl)-3,4,6,7-tetrahydro-2H-pyrimido[6,1-a]isoquinolin-4-one (preparation given) in aqueous
HCl at 80° followed by stirring for 2 h to give 54% 9,10-dimethoxy-2-(2,4,6-trimethylphenylimino)-3-(N-carbamoyl-2-aminoethyl)-3,4,6,7-tetrahydro-2H-pyrimido[6,1-a]isoquinolin-4-one(II). II inhibited PDE3 with IC50 = 0.46 μM and was tasteless.

SUPPL. TERM: aryliminopyrimidoisoquinolinone prepn phosphodiesterase inhibitor; pyrimidoisoquinolinone arylimino prepn phosphodiesterase inhibitor; chronic obstructive pulmonary disease treatment aryliminopyrimidoisoquinolinone prepn; antiasthmatic aryliminopyrimidoisoquinolinone prepn; bronchodilator aryliminopyrimidoisoquinolinone prepn

INDEX TERM: Lung, disease

(chronic obstructive, treatment; preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)

INDEX TERM: Antiasthmatics
Bronchodilators
Cytotoxic agents
(preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)

INDEX TERM: Proliferation inhibition
(proliferation inhibitors; preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)

INDEX TERM: Tumor necrosis factors
ROLE: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(release inhibitors; preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)

INDEX TERM: 9036-21-9, Phosphodiesterase III
ROLE: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(inhibitors; preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)

INDEX TERM: **298680-25-8P 298680-26-9P**
298680-27-0P 298680-28-1P
298680-29-2P 298680-30-5P
298680-31-6P 298680-32-7P
298680-33-8P 298680-34-9P
298680-35-0P 298680-36-1P
298680-37-2P
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)

INDEX TERM: 62-56-6, Thiourea, reactions 75-31-0, Isopropylamine, reactions 88-05-1, 2,4,6-Trimethylaniline 95-53-4, 2-Methylaniline, reactions 103-71-9, Phenyl isocyanate, reactions 574-98-1, N-(2-Bromoethyl)phthalimide 1795-48-8, Isopropyl isocyanate 2260-00-6 3173-53-3, Cyclohexyl isocyanate 5394-18-3, N-(4-Bromobutyl)phthalimide 10191-60-3, Dimethyl N-cyanodithioiminocarbonate 13623-94-4 24544-04-5, 2,6-Diisopropylaniline 61832-41-5 **298680-49-6**
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)

INDEX TERM: 2986-25-6P **75535-96-5P 76536-66-8P**
145013-05-4P **214358-62-0P 298680-38-3P**
298680-39-4P 298680-40-7P
298680-41-8P 298680-42-9P
298680-43-0P 298680-44-1P
298680-45-2P 298680-46-3P
298680-47-4P 298680-48-5P
298680-50-9P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)

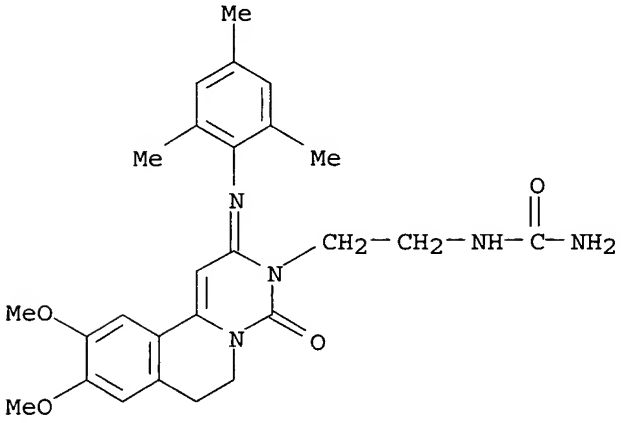
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S): (1) Bansai, L; JOURNAL OF MEDICINAL CHEMISTRY 1984, V27(11), P1470

IT **298680-25-8P 298680-26-9P 298680-27-0P**
298680-28-1P 298680-29-2P 298680-30-5P
298680-31-6P 298680-32-7P 298680-33-8P
298680-34-9P 298680-35-0P 298680-36-1P
298680-37-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)

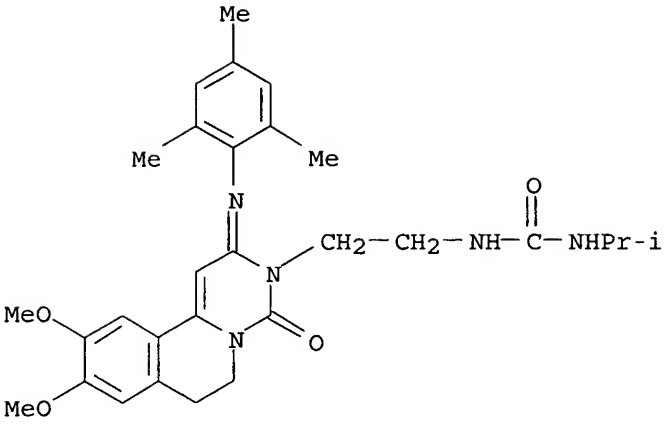
RN 298680-25-8 HCAPLUS

CN Urea, [2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)

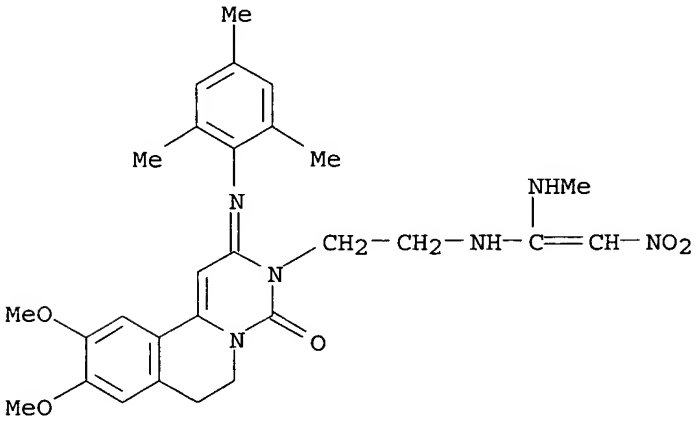


RN 298680-26-9 HCAPLUS

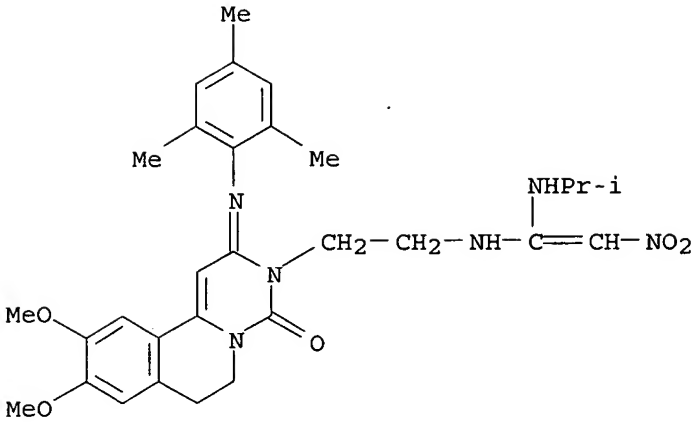
CN Urea, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-(1-methylethyl)- (9CI) (CA INDEX NAME)



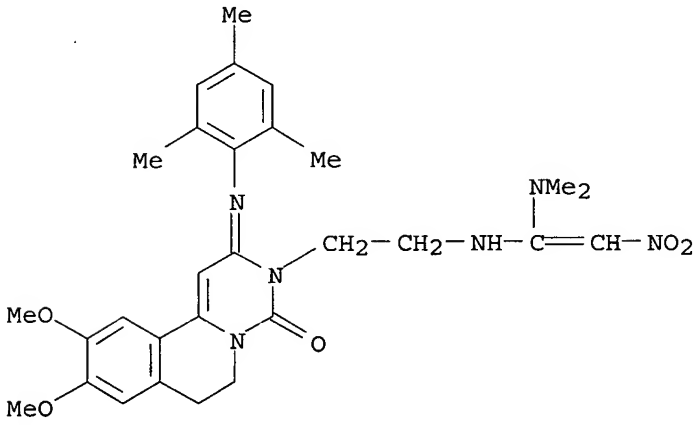
RN 298680-27-0 HCAPLUS
CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 2,3,6,7-tetrahydro-9,10-dimethoxy-3-[2-[[1-(methylamino)-2-nitroethenyl]amino]ethyl]-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)



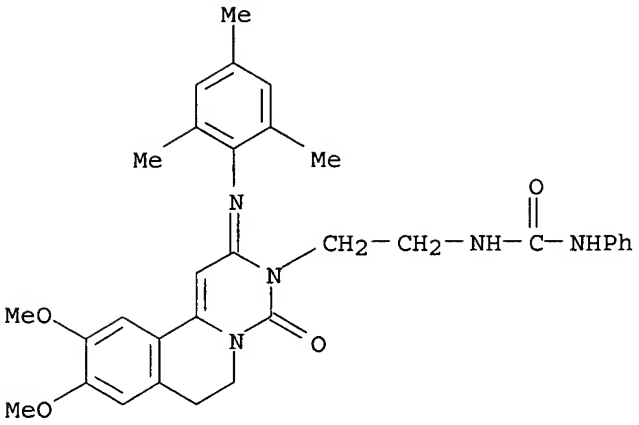
RN 298680-28-1 HCAPLUS
CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 2,3,6,7-tetrahydro-9,10-dimethoxy-3-[2-[[1-[(1-methylethyl)amino]-2-nitroethenyl]amino]ethyl]-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)



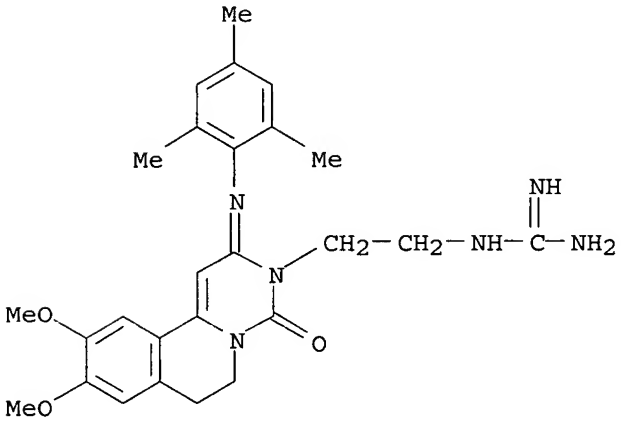
RN 298680-29-2 HCAPLUS
CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 3-[2-[[1-(dimethylamino)-2-nitroethenyl]amino]ethyl]-2,3,6,7-tetrahydro-9,10-dimethoxy-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)



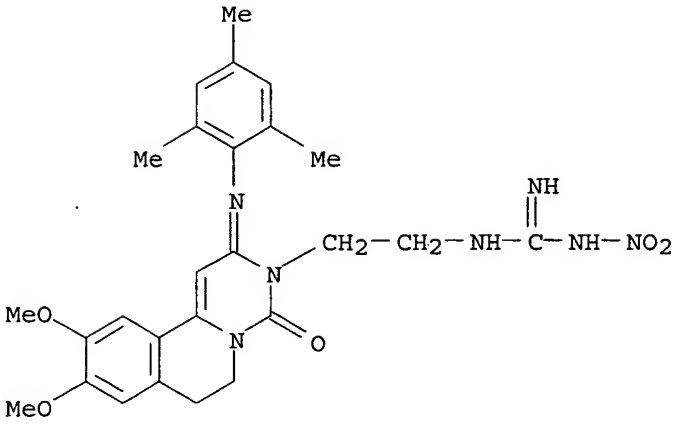
RN 298680-30-5 HCAPLUS
CN Urea, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-phenyl- (9CI) (CA INDEX NAME)



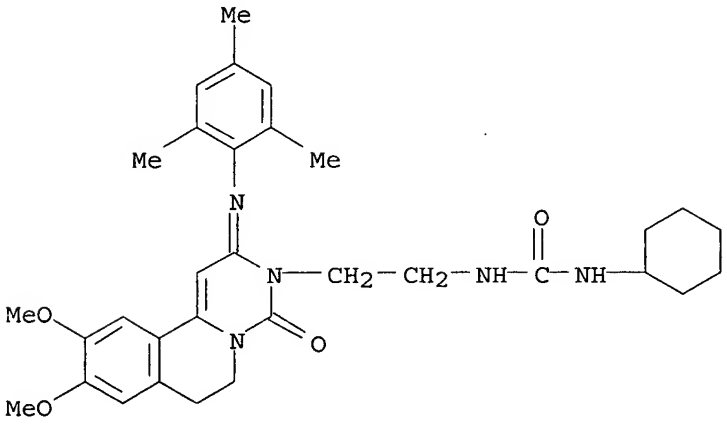
RN 298680-31-6 HCAPLUS
CN Guanidine, [2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)



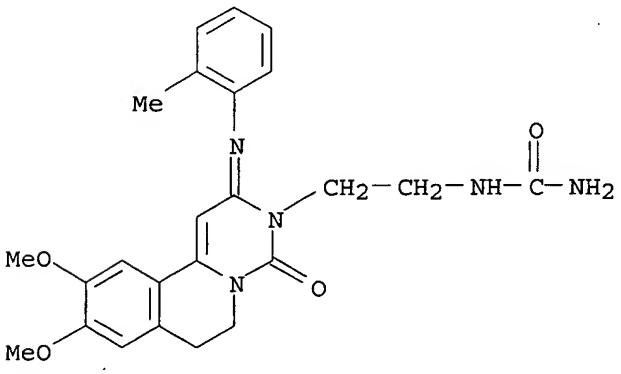
RN 298680-32-7 HCAPLUS
CN Guanidine, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-nitro- (9CI) (CA INDEX NAME)



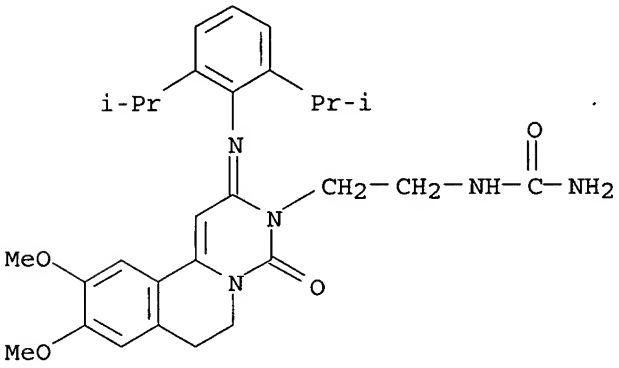
RN 298680-33-8 HCAPLUS
CN Urea, N-cyclohexyl-N'-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)



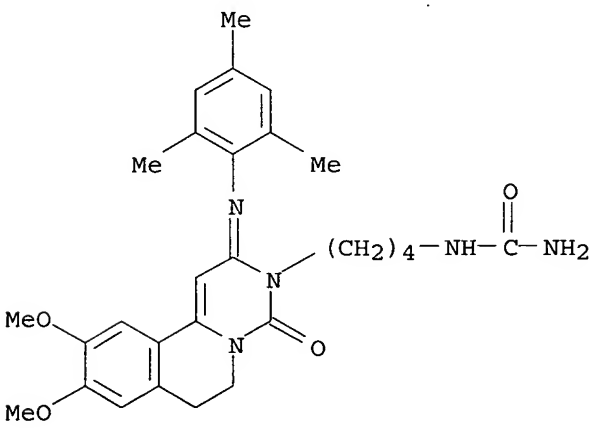
RN 298680-34-9 HCAPLUS
CN Urea, [2-[6,7-dihydro-9,10-dimethoxy-2-[(2-methylphenyl)imino]-4-oxo-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)



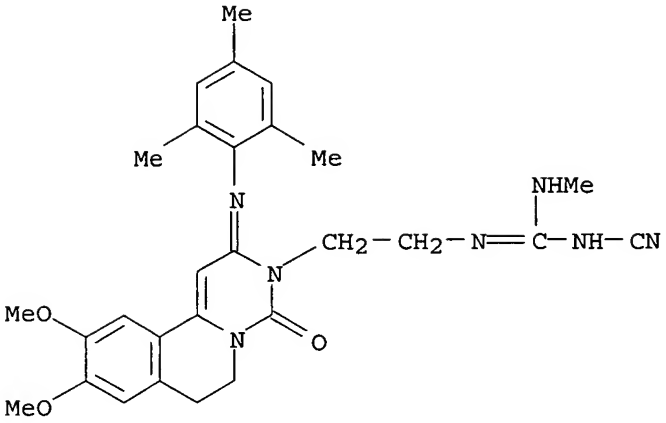
RN 298680-35-0 HCAPLUS
CN Urea, [2-[2-[[2,6-bis(1-methylethyl)phenyl]imino]-6,7-dihydro-9,10-dimethoxy-4-oxo-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)



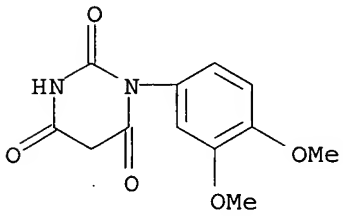
RN 298680-36-1 HCAPLUS
CN Urea, [4-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]butyl]- (9CI) (CA INDEX NAME)



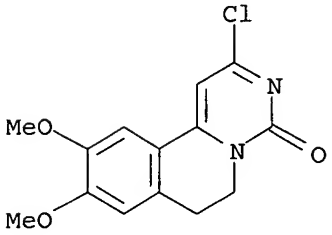
RN 298680-37-2 HCAPLUS
CN Guanidine, N-cyano-N'-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N''-methyl- (9CI) (CA INDEX NAME)



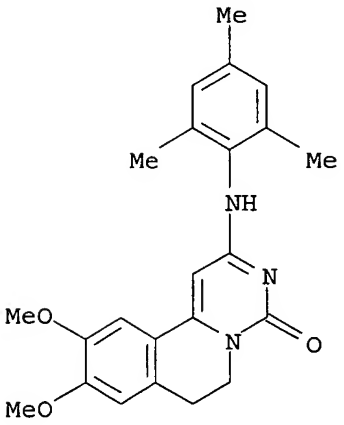
IT **298680-49-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)
RN 298680-49-6 HCAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 1-(3,4-dimethoxyphenyl)- (9CI) (CA INDEX NAME)



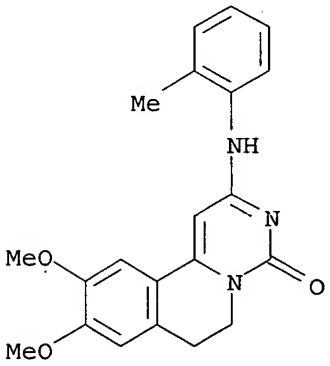
IT **75535-96-5P 76536-66-8P 214358-62-0P**
298680-38-3P 298680-39-4P 298680-40-7P
298680-41-8P 298680-42-9P 298680-43-0P
298680-44-1P 298680-45-2P 298680-46-3P
298680-47-4P 298680-48-5P 298680-50-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)
RN 75535-96-5 HCAPLUS
CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 2-chloro-6,7-dihydro-9,10-dimethoxy- (9CI) (CA INDEX NAME)



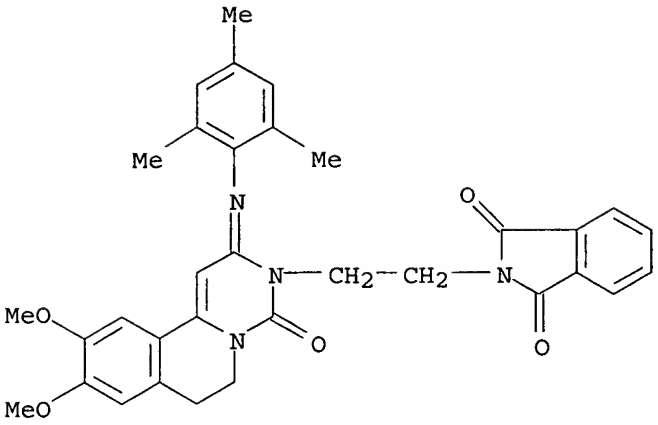
RN 76536-66-8 HCAPLUS
CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 6,7-dihydro-9,10-dimethoxy-2-[(2,4,6-trimethylphenyl)amino]- (9CI) (CA INDEX NAME)



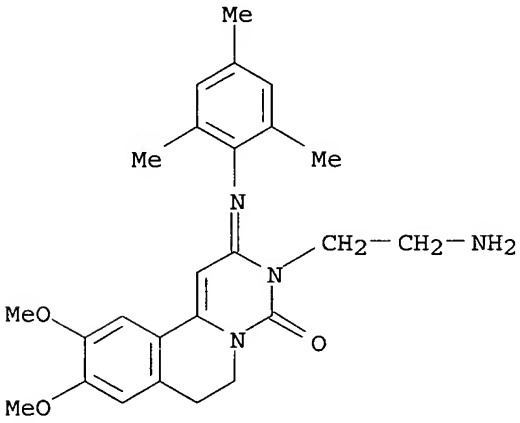
RN 214358-62-0 HCAPLUS
CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 6,7-dihydro-9,10-dimethoxy-2-[(2-methylphenyl)amino]- (9CI) (CA INDEX NAME)



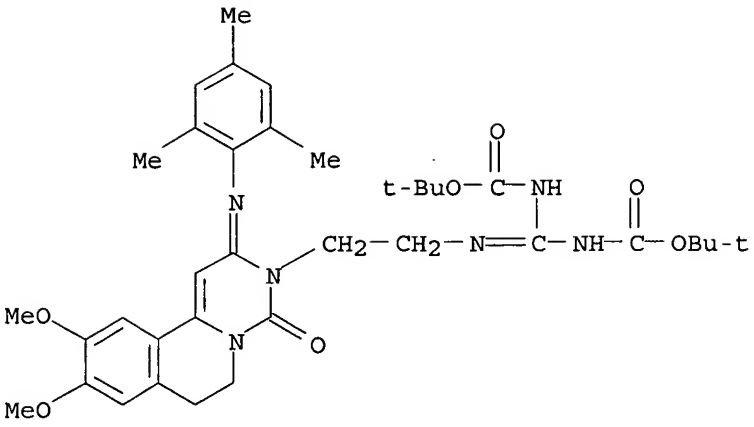
RN 298680-38-3 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)



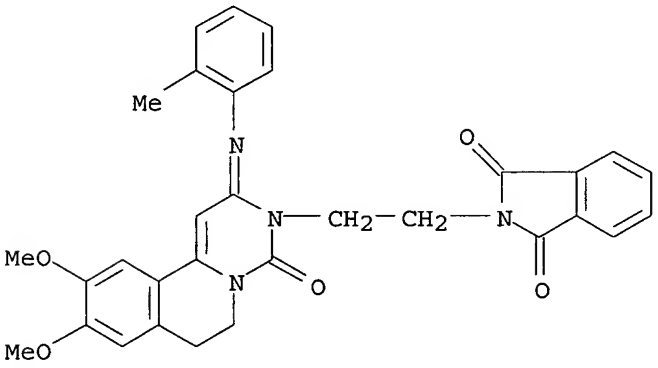
RN 298680-39-4 HCAPLUS
CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 3-(2-aminoethyl)-2,3,6,7-tetrahydro-9,10-dimethoxy-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)



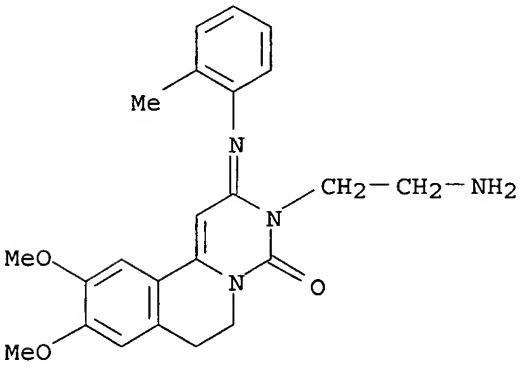
RN 298680-40-7 HCAPLUS
CN Carbamic acid, [[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]carbonimidoyl]bis-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



RN 298680-41-8 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[6,7-dihydro-9,10-dimethoxy-2-[(2-methylphenyl)imino]-4-oxo-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)

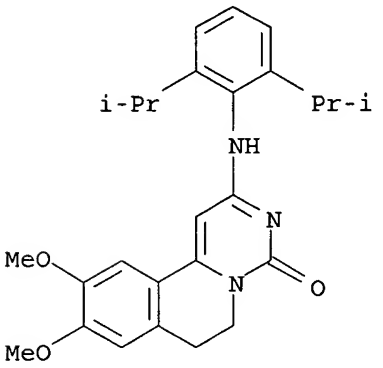


RN 298680-42-9 HCAPLUS
CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 3-(2-aminoethyl)-2,3,6,7-tetrahydro-9,10-dimethoxy-2-[(2-methylphenyl)imino]- (9CI) (CA INDEX NAME)

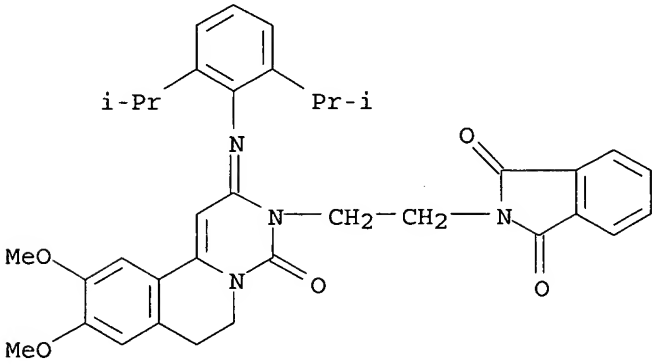


RN 298680-43-0 HCAPLUS

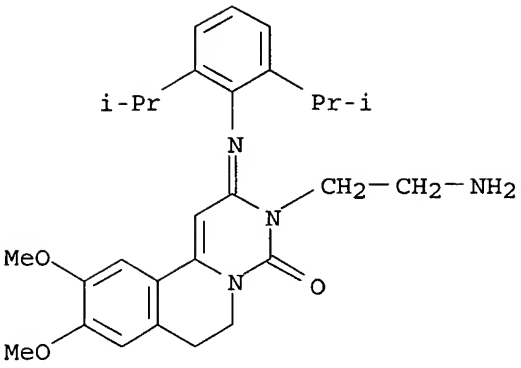
CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 2-[[2,6-bis(1-methylethyl)phenyl]amino]-6,7-dihydro-9,10-dimethoxy- (9CI) (CA INDEX NAME)



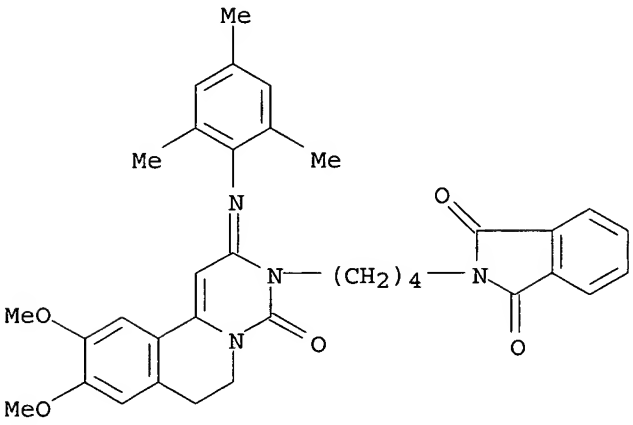
RN 298680-44-1 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[2-[[2,6-bis(1-methylethyl)phenyl]imino]-6,7-dihydro-9,10-dimethoxy-4-oxo-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)



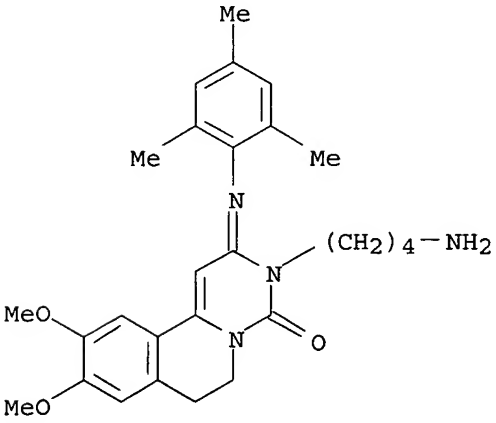
RN 298680-45-2 HCAPLUS
CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 3-(2-aminoethyl)-2-[[2,6-bis(1-methylethyl)phenyl]imino]-2,3,6,7-tetrahydro-9,10-dimethoxy- (9CI) (CA INDEX NAME)



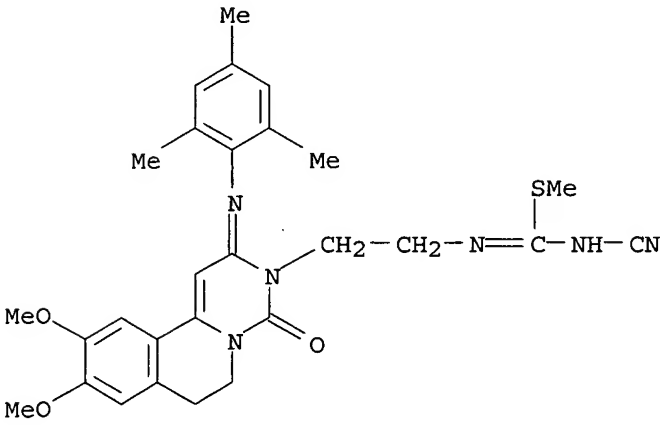
RN 298680-46-3 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[4-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]butyl]- (9CI) (CA INDEX NAME)



RN 298680-47-4 HCAPLUS
CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 3-(4-aminobutyl)-2,3,6,7-tetrahydro-9,10-dimethoxy-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)



RN 298680-48-5 HCAPLUS
CN Carbamimidothioic acid, N-cyano-N'-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 298680-50-9 HCAPLUS
CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 2,3,6,7-tetrahydro-9,10-dimethoxy-3-[2-[[1-(methylthio)-2-nitroethenyl]amino]ethyl]-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)